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Middeldorp, C.M.; Cath, D.C.; van den Berg, M.; Beem, A.L.; van Dyck, R.; Boomsma, D.I.

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The Association of Personality with Anxious and Depressive Psychopathology

Christel M. Middeldorp, Danielle C. Cath, Mireille van den Berg, A. Leo Beem, Richard van Dyck, and Dorret I. Boomsma

The questions of to what extent and in which ways personality dimensions are associated with anxious and depressive psychopathology are still unresolved. Most research has focused on "neuroticism" and "extraversion," or traits related to these personality dimensions. Neuroticism was originally described as reflecting emotional instability and anxiety proneness (Eysenck & Rachman, 1965). This trait was hypothesized to be related to the "visceral brain," more often called the "limbic system," which was supposed to regulate emotional expression and to control autonomic responses. According to Eysenck (1967), neurotic subjects are characterized by higher levels of autonomic activity (or reactivity), mediated by the visceral brain.

Extraversion was described as reflecting sociability, liveliness, impulsivity, and the level of ease and pleasure felt in the company of others (Eysenck & Rachman, 1965). The last-mentioned trait was theorized to be related to the ascending reticular activating system, with a higher level of arousal in introverts and a higher level of inhibition in extraverts (Eysenck, 1967). A wide range of electrophysiological and other psychophysiological studies confirmed this hypothesis (Stelmack, 1981).

Cloninger (1986) proposed that "harm avoidance," an anxiety-related trait, is positioned between neuroticism and extraversion. This positioning was confirmed by a strong positive correlation with neuroticism (r = .63) and a strong negative correlation with extraversion (r = –.55), as measured with

the Eysenck Personality Questionnaire (EPQ) (see Heath, Cloninger, & Martin, 1994).

Two dimensions that are related to neuroticism and extraversion are "positive affectivity" and "negative affectivity." Negative affectivity is a general dimension of subjective distress and unpleasurable engagement, whereas positive affectivity reflects the extent to which a person feels enthusiastic, active, and alert (Watson, Clark, & Tellegen, 1988). There is general consensus that individuals scoring high on neuroticism exhibit negative affectivity (Shankman & Klein, 2003). Therefore, "negative affectivity" and "neuroticism" are often used interchangeably in the literature. However, this does not hold for the relation between extraversion and positive affectivity. Since extraversion does not only measure positive affectivity, but also impulsivity and sociability, this dimension encompasses more than positive affectivity only (Clark, Watson, & Mineka, 1994).

A further personality trait is "sensation seeking," which was considered to be a measure of the impulsivity and sociability parts of Eysenck's broader extraversion dimension and to be independent of neuroticism (Zuckerman, 1979). Zuckerman (1979) defined this trait as "the need for varied, novel, and complex sensations and experiences and the willingness to take physical and social risks for the sake of such experience" (p. 10). Sensation seeking was also supposed to be related to an individual's level of arousal. Different studies investigating the relation between sensation seeking and Eysenck's personality dimensions found correlations between extraversion and sensation seeking from .09 to .42 in men and from .11 to .44 in women (Zuckerman, 1979). The correlations of neuroticism and sensation seeking were nonsignificant (Zuckerman, 1979).

Several hypotheses regarding the relationships of these personality dimensions to anxious and/or depressive psychopathology have been put forward. Eysenck and Rachman (1965) hypothesized that subjects with symptoms of anxiety and/or depression would be high in neuroticism and low in extraversion. Gray (1982) suggested that these two dimensions could be combined into one trait, reflecting the level of activity in the behavioral inhibition system and indicating a person's vulnerability for anxiety and depression. This led to the harm avoidance dimension (Cloninger, 1986). Clark and Watson (1991) developed the tripartite model, which agrees with Eysenck's model that negative affectivity is a risk factor for both anxiety and depression. However, according to the tripartite model, low positive affectivity is related to depression only, whereas autonomic hyperarousal (e.g., racing heart, trembling, shortness of breath, dizziness) is related to anxiety. Finally, sensation seeking was hypothesized to be unrelated to depression and anxiety disorders, since it is not associated with neuroticism (Zuckerman, 1979).

Research so far has confirmed that negative affectivity/neuroticism is related to both depression and anxiety (for reviews, see Bienvenu & Stein, 2003; Clark et al., 1994; Shankman & Klein, 2003). This also applies to harm avoidance (Brown, Svrakic, Przybeck, & Cloninger, 1992; Cloninger, 2002;

Shankman & Klein, 2003). Results have been contradictory concerning the association between low positive affectivity/extraversion and depression or anxiety disorders (see Shankman & Klein, 2003, for a review). A possible source of confounding, which is not taken into account in most studies, is the highly prevalent comorbidity between anxiety and depression. If, for example, high neuroticism is a risk factor for both anxiety and depression, but low extraversion only for depression (as supposed in the tripartite model), it may be hypothesized that subjects with pure anxiety disorders are only high in neuroticism, while subjects with both anxiety and depression are low in extraversion as well. As a consequence, whether or not a study focusing on anxiety observes that low extraversion is related to anxiety will depend on the number of subjects with comorbid anxiety and depression. This is just one example of how comorbidity may modify the association between personality and psychopathology.

Several approaches can be used to take comorbidity into account when investigators are examining the association between personality and psychopathology. One way is to study subjects with the pure disorders separately from the subjects with the comorbid condition. Another possibility is to compare the mean scores on personality dimensions of normal controls and affected subjects while correcting for comorbid disease. For example, in an analysis of variance (ANOVA) or a regression analysis, all disorders can be included in one model. Finally, factor analyses or structural equation modeling can be used to investigate the etiology of the correlation between measures of personality and anxious or depressive psychopathology.

In all studies taking these approaches, neuroticism was related to major depression and anxiety disorders (Bienvenu et al., 2001; Brown, Chorpita, & Barlow, 1998; de Graaf, Bijl, ten Have, Beekman, & Vollebergh, 2004; Johnson, Turner, & Iwata, 2003; Krueger, McGue, & Iacono, 2001; Trull & Sher, 1994). In addition, all studies except one (Johnson et al., 2003) found a relation between low extraversion and one or more of the anxiety disorders, although results were not always consistent on the level of specific diagnoses (Bienvenu et al., 2001; Brown et al., 1998; Trull & Sher, 1994). Results were contradictory regarding the relation between low extraversion and major depression. Brown and colleagues (1998) and Trull and Sher (1994) did find an association, whereas Bienvenu and colleagues (2001) and Johnson and colleagues (2003) did not. Krueger and colleagues (2001) found that internalization—a factor on which depression and anxiety disorders loaded—correlated negatively with positive emotionality in women, but not in men. These studies also revealed that comorbidity between anxiety and depression is associated with neuroticism (Andrews, Slade, & Issakidis, 2002; Bienvenu et al., 2001; de Graaf et al., 2004) and, to a limited extent, with low extraversion (Bienvenu et al., 2001). Andrews and colleagues (2002) even found a linear relationship between neuroticism and the number of disorders. To summarize, studies that take comorbidity into account find in general that high neuroticism and low extraversion are related to depression as well as

anxiety; this is in agreement with Eysenck's theory and in contradiction to the tripartite model.

The association between sensation seeking and anxious or depressive psychopathology has been studied far less often, and results are contradictory. To our knowledge, no previous studies have investigated this relation while taking comorbidity into account. Zuckerman (1979) concluded that although there is no association between sensation seeking and depression or general trait anxiety, sensation seeking could be negatively related to fearfulness of more specific types. However, in two recent studies, low levels of sensation seeking appeared to be related to major depression (Carton, Morand, Bungenera, & Jouvent, 1995; Farmer et al., 2001).

In this chapter, we describe two studies that investigated the relationship between the personality dimensions of neuroticism, extraversion, and sensation seeking on the one hand, and anxiety and depression on the other. In both studies, comorbidity was taken into account. The goals of these studies were to test whether Eysenck's model or the tripartite model best describes the data, and to test the extent to which sensation seeking is related to anxious and depressive psychopathology. The latter issue is interesting, because Zuckerman (1979) based his hypothesis that sensation seeking is not associated to anxiety and depression on the absence of a correlation between neuroticism and sensation seeking. However, as he also acknowledged, sensation seeking is correlated with extraversion. Since low extraversion may be related to anxiety and depression, this could be the case for sensation seeking as well.

The first study was based on self-report questionnaire data of personality and psychopathology from twins and their siblings registered in the Netherlands Twin Register (NTR). In 1991, 1993, and 1997, a survey was sent to twins; in 1997, their siblings were also approached. These three waves were combined for the analyses, in order to obtain one of the largest samples so far used to investigate the association of neuroticism, extraversion, and sensation seeking with symptoms of anxiety and depression. Correlations were calculated within and between the personality and psychopathology dimensions. Furthermore, to take comorbidity into account, subjects were divided into cases and normal controls on the measures of anxiety and depression, with the 95th percentile used as a cutoff score. Next, the mean scores on the personality measures of the pure cases and the comorbid cases were compared with the means of the normal controls.

In the second study, data from a diagnostic psychiatric interview administered to a selected sample of twins and their siblings were analyzed. Scores on neuroticism, extraversion, and sensation seeking were compared between subjects without psychopathology and subjects with depression or an anxiety disorder defined according to the *Diagnostic and Statistical Manual of Mental Disorders*, fouth edition (DSM-IV; American Psychiatric Association, 1994). This analysis was performed while correcting for comorbidity, by comparing the means between normal controls and affected subjects with all disorders

included in the same model. Finally, mean personality scores were compared between subjects with zero, one, two, or three or more disorders. The two studies are described separately, followed by an overall discussion.

STUDY I: THE ASSOCIATION OF PERSONALITY WITH ANXIOUS AND DEPRESSIVE PSYCHOPATHOLOGY MEASURED DIMENSIONALLY

The first study was part of an ongoing longitudinal survey study of the NTR, which has assessed families with adolescent and adult twins roughly every 2 years since 1991. Sample selection and response rates are described in detail in Boomsma and colleagues (2002). Each survey was sent to the twins and additional family members—namely, parents in 1991 and 1993, parents and siblings in 1995, and siblings in 1997. Each survey, with the exception of the 1995 wave, collected information on personality and psychopathology. For this study, data from twins and siblings from the 1991, 1993, and 1997 surveys were used. In these years, questionnaires were returned at least once by 2,825 male and 3,636 female twins, and 668 brothers and 840 sisters, from 3,349 families. Forty-two percent of the subjects participated two or three times, and 58% participated once. The mean ages of the subjects at the time of the three waves were 18, 20, and 27 years, with standard deviations 2.3, 8.4, and 10.5 years, respectively.

On all three occasions, sensation seeking was measured with the Dutch translation of the Zuckerman Sensation Seeking Scale (Feij & van Zuilen, 1984; Zuckerman, 1971). Neuroticism, extraversion, and somatic anxiety were measured with the Amsterdamse Biografische Vragenlijst (ABV; Wilde, 1970). The ABV Neuroticism and Extraversion scales are very similar to those of the EPQ (Eysenck & Eysenck, 1964). Somatic anxiety is measured with items such as "Do you often have a headache?" and "Do you have heart palpitations?" Anxiety was measured with the Dutch translation of the Spielberger State–Trait Anxiety Inventory—Trait version (STAI; Spielberger, Gorsuch, & Lushene, 1970; Van der Ploeg, Defares, & Spielberger, 1979). Depression was measured with two different inventories in the three surveys. In 1991, the Anxious/Depressed symptom scale of the Young Adult Self-Report (YASR; Achenbach, 1990; Verhulst, van Ende, & Koot, 1997) was used; in 1993, the 13-item version of the Beck Depression Inventory (BDI; Beck, Rial, & Rickels, 1974) was used; and in 1997, both instruments were used.

For all personality and psychopathology measures, normalized scores were calculated according to Blom's (1958) methods, so that we could compare the scores across scales and time. These scores were averaged over time when a subject had participated more than once in the survey study. Figures 12.1a to 12.1g show the distributions of the mean normalized scores for neu-

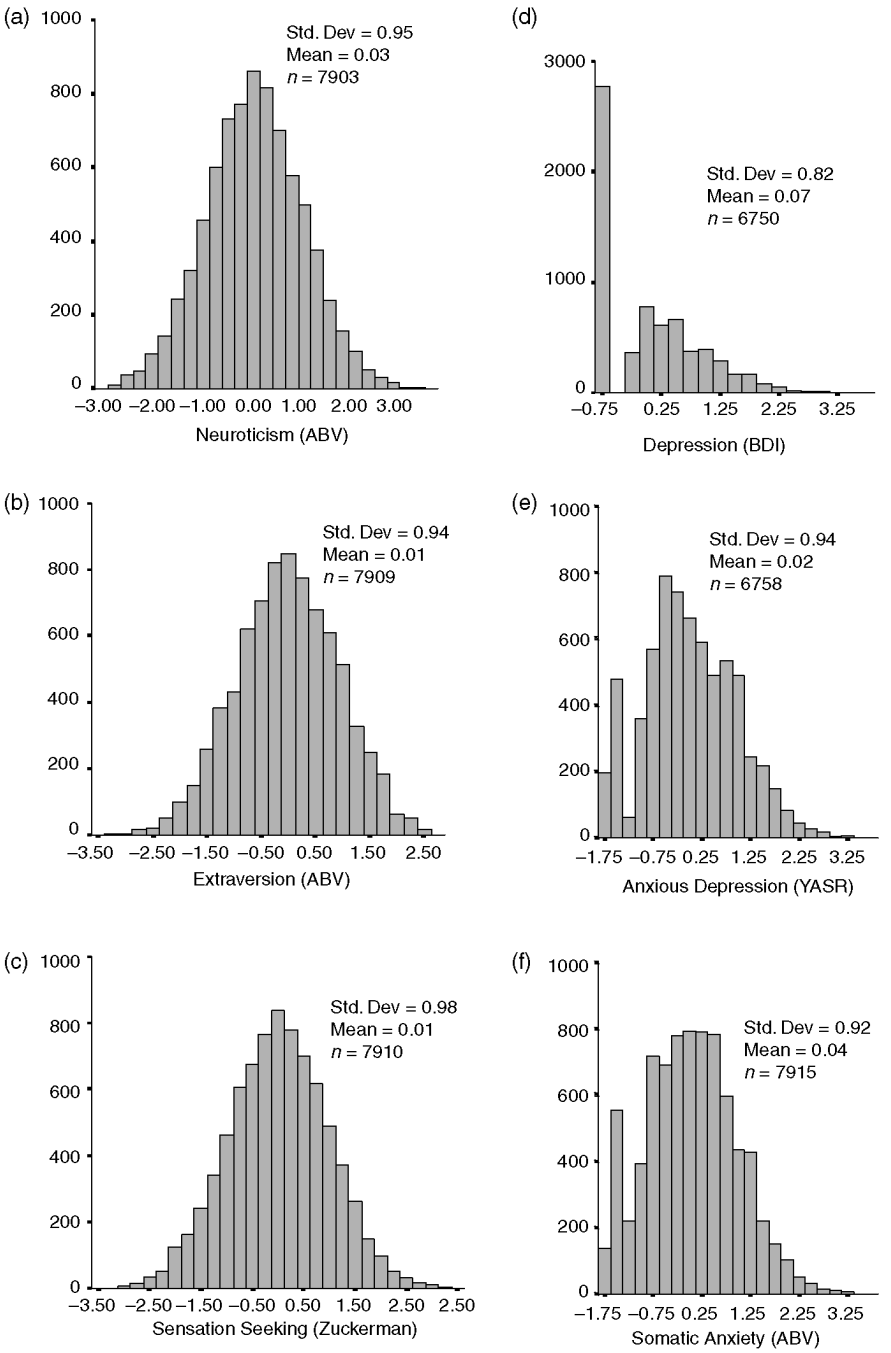

FIGURE 12.1. Distributions of personality and psychopathology normalized scores and genetic factor scores.

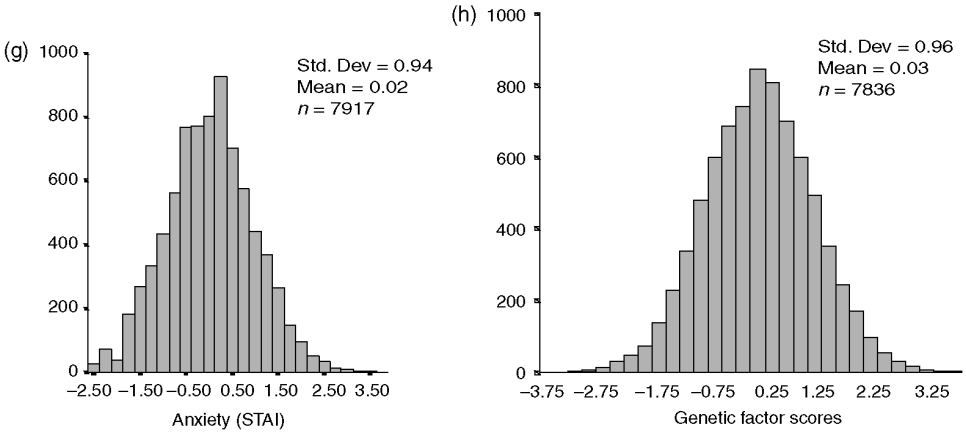

FIGURE 12.1. *(continued)*

roticism, extraversion, sensation seeking, depression, anxious depression, somatic anxiety, and anxiety, respectively. All variables were more or less normally distributed, with the exception of the depression scores.

Mean scores were compared between sexes with student's *t*-test. All dimensions differed significantly ($p < .0001$) between men and women, with men scoring lower on neuroticism and all psychopathology measures, and higher on extraversion and sensation seeking (Table 12.1).

Pearson correlations were calculated within and between the personality and psychopathology dimensions for men and women separately. The correlations within and between the personality and psychopathology dimensions were all significant at the level of alpha < .01 (Table 12.2). It is clear that mea-

TABLE 12.1. Mean Raw and Normalized Scores and Standard Deviations for Neuroticism, Extraversion, Sensation Seeking (Total Score), Beck Depression Inventory, Anxious Depression, Somatic Anxiety, and Anxiety for Men and Women

	Men		Women	
	Raw (*SD*)	Normalized (*SD*)	Raw (*SD*)	Normalized (*SD*)
Neuroticism	46.59 (21.34)	–0.19 (0.92)	55.18 (23.38)	0.19 (0.94)
Extraversion	60.77 (15.32)	0.03 (0.96)	59.88 (15.16)	–0.05 (0.93)
Sensation seeking	11.74 (1.75)	0.33 (0.91)	10.59 (1.91)	–0.24 (0.95)
Depression	1.30 (2.21)	–0.07 (0.77)	1.98 (2.84)	0.17 (0.85)
Anxious depression	3.77 (3.57)	–0.22 (0.86)	5.65 (4.59)	0.20 (0.96)
Somatic anxiety	17.55 (4.71)	–0.10 (0.87)	18.85 (5.43)	0.14 (0.94)
Anxiety	31.90 (7.50)	–0.13 (0.91)	34.27 (8.59)	0.15 (0.95)

TABLE 12.2. Correlations for Neuroticism, Extraversion, Total Score on Sensation Seeking, Beck Depression Inventory, Somatic Anxiety, Anxious Depression, and Anxiety for Men (Upper Diagonal) and Women (Lower Diagonal)

	Neu	Ext	SSS	BDI	AD	SoA	Anx
Neu		–.22	.19	.53	.60	.59	.69
Ext	–.22		.36	–.18	–.23	–.12	–.24
SSS	.18	.31		.08	.08	.17	.13
BDI	.58	–.20	.08		.48	.40	.58
AD	.70	–.27	.10	.56		.42	.61
SoA	.61	–.19	.13	.46	.48		.47
Anx	.75	–.22	.14	.65	.71	.53	

Note. Neu, neuroticism; Ext, extraversion; SSS, sensation seeking (total score); BDI, Beck Depression Inventory; AD, anxious depression; SoA, somatic anxiety; Anx, anxiety.

sures of anxiety and depression were highly correlated. Moderate correlations were seen within the personality measures, with a negative correlation between neuroticism and extraversion. Regarding the relation between personality and psychopathology, neuroticism showed high correlations with anxiety as well as depression, while extraversion was (to a lesser extent) negatively correlated with these symptoms. Sensation seeking did not appear to be related to any of these measures, and especially not to depression. Finally, these conclusions were very similar for men and women, with no differences in the size of the correlations.

Correlations among the psychopathology measures were high, and it was possible that the correlations between the personality measures of neuroticism and extraversion and all the psychopathology measures were due to just one of the psychopathology dimensions. Therefore, for the four psychopathology measures (depression [BDI], anxious depression [YASR], somatic anxiety [ABV], and anxiety [STAI]), the population was divided into cases and normal controls, with the 95th percentile as a cutoff score. Cases were further divided into subjects with pure "disorders" and with comorbid conditions. This led to 15 groups of cases, as summarized in Table 12.3 (e.g., one group with cases of pure depression, one group of cases with depression and somatic anxiety, etc.). Since subjects had to have a score on all four instruments to be categorized in one of the groups, 2416 subjects were excluded from this analysis. In a multivariate analysis of variance (MANOVA), personality scores for each group of cases were compared with those for the normal controls. Table 12.3 shows that all groups of cases had significantly higher neuroticism scores than the normal controls ($p < .0001$), and that almost all groups of cases had significantly lower extraversion scores ($p < .0001$ or $p < .001$), whereas just one group scored significantly higher on sensation seeking ($p < .05$).

TABLE 12.3. Mean Scores and Standard Deviations for Neuroticism, Extraversion, and Sensation Seeking (Total Score) for the Nondisordered Controls and the 14 Groups of Cases with Scores above the 95th Percentile on Depression, Anxious Depression, Somatic Anxiety, and/or Anxiety

	n	Neu (*SD*)	Ext (*SD*)	SSS (*SD*)
Controls	4994	–0.16 (0.83)	0.05 (0.92)	–0.03 (0.96)
BDI	90	0.86 (0.56)***	–0.31 (0.93)***	0.02 (0.93)
AD	95	1.09 (0.58)***	–0.46 (1.03)***	0.09 (1.05)
SoA	98	1.01 (0.71)***	–0.20 (0.96)**	–0.07 (1.07)
Anx	35	1.33 (0.53)***	–0.54 (0.97)***	–0.05 (0.93)
BDI + AD	14	1.41 (0.41)***	–0.86 (0.86)***	0.07 (0.73)
BDI + SoA	17	1.01 (0.51)***	–0.59 (0.97)**	0.19 (1.22)
BDI + Anx	25	1.48 (0.45)***	–0.23 (0.84)	–0.27 (1.04)
AD + SoA	9	1.40 (0.55)***	–0.37 (0.79)	0.37 (0.58)
AD + Anx	41	1.72 (0.49)***	–0.50 (0.81)***	0.28 (0.91)*
SoA + Anx	14	1.74 (0.50)***	–0.64 (0.94)**	–0.26 (1.20)
BDI + AD + SoA	11	1.40 (0.56)***	–0.96 (0.99)***	–0.08 (1.23)
BDI + AD + Anx	39	1.72 (0.62)***	–0.75 (0.92)***	0.01 (0.94)
BDI + SoA + Anx	18	1.82 (0.55)***	–0.87 (0.91)***	0.32 (0.98)
AD + SoA + Anx	10	1.93 (0.25)***	–0.33 (0.40)	–0.20 (1.03)
BDI + AD + SoA + Anx	43	2.11 (0.48)***	–0.89 (0.91)***	–0.01 (0.96)

Note. Abbreviations as in Table 12.2.
*$p < .05$ versus controls; **$p < .001$ versus controls; *** $p < .0001$ versus controls.

STUDY II: THE ASSOCIATION OF PERSONALITY WITH PSYCHOPATHOLOGY CATEGORIZED ACCORDING TO DSM-IV DIAGNOSES

In 1998, we performed a selection to obtain a subsample of twin families that would be informative for a linkage study to localize the genes underlying the susceptibility to anxiety and depression. The selection strategy was based on the recommendation of Eaves and Meyer (1994) and Risch and Zhang (1995) to select sibling pairs for genotyping with extreme scores (high–high, low–low, low–high, or high–low) on a quantitative scale of interest. Simulation studies have shown the optimal selection percentages for linkage analysis in sibling pairs from random samples (Dolan & Boomsma, 1998). Concordant sibling pairs were selected when both had scores in the top 12% or in the bottom 12% of the phenotypic distribution. For discordant pairs, an "asymmetrical" criterion appeared to be optimal. Discordant sibling pairs were selected if one sibling had a score in the top 25% and the other in the bottom 20%, or if one had a score in the top 20% and the other in the bottom 25%. The quanti-

tative scale used for the selection consisted of a genetic factor score expressing a subject's genetic susceptibility to "anxious depression." The formula to calculate these factor scores was derived from a multivariate genetic analysis on the anxiety, depression, neuroticism, and somatic anxiety data collected for twins and their siblings in 1991, 1993, and 1997. This analysis revealed that covariances for these traits could be fully attributed to a common genetic factor (Boomsma et al., 2000). The value of this common genetic factor could be estimated for each individual by using the individual scores on the traits and the factor loadings on the common genetic factor. Since the factor loadings on the common genetic factor were different for males and females, the formulas to estimate the genetic factor score were different for males and females. Furthermore, genetic factor scores depended on whether the BDI or the YASR depression scale was used in the construction. For example, this was the formula for males when the score on the YASR was used: Genetic factor score = 0.144 × anxiety + 0.117 × neuroticism + 0.039 × somatic anxiety + d.064 × depression (YASR). More detailed information on how the factor scores were calculated is provided elsewhere (Boomsma et al., 2000). The correlation between the factor scores calculated with the score on the BDI and the score on the YASR in the 1997 survey was .98.

A factor score could be calculated for 7,836 twins and siblings who participated at least once in the 1991, 1993, or 1997 survey (see Figure 12.1h). Subjects who missed one or more of the inventories that measured neuroticism, anxiety, somatic anxiety, or depression were excluded. Based on these factor scores, 561 families were selected in which both members of a sibling pair had extreme factor scores. All members of the selected families, regardless of their genetic factor scores, were asked to provide a buccal swab for DNA isolation. Twins and siblings in these families were also asked to participate in a diagnostic psychiatric interview. For example, in monozygotic twin pairs in which one (or both) of the twins formed an extreme pair with an additional sibling, both the twins and the additional sibling were invited to take part in the study. Finally, a subsample of concordant and discordant monozygotic twins and seven unselected families participated in the interview. In 143 families, not all family members were approached. Eventually, 332 male and 504 female twins, and 193 brothers and 227 sisters, from 479 families were interviewed. One hundred and seven subjects were not available (e.g., because the phone was not answered several times), and 154 subjects refused to participate.

Table 12.4 shows the consequences of the selection on the distribution of the factor scores on an individual level. Eighty percent of the interviewed subjects had extreme scores (i.e., above the 75th or below the 25th percentile of the total population). Subjects who refused to participate had less extreme scores than the subjects who participated, whereas subjects who were not available for the interview had more extreme scores. For 17 twins and siblings, no genetic factor score was available. They were asked to participate in the interview because they were family members of an extreme-scoring sibling

TABLE 12.4. Interview Participation and Factor Scores

	Not approached (*n*/%)	Participated (*n*/%)	Refused participation (*n*/%)	Respondent not available (*n*/%)
fs ≥ 75th %	1803 (28.5%)	460 (37.1%)	45 (29.4%)	52 (48.6%)
fs ≤ 25th %	1671 (26.4%)	480 (38.7%)	70 (45.8%)	34 (31.8%)
fs between 25th % and 75th %	2808 (44.3%)	256 (20.6%)	31 (20.3%)	20 (18.7%)
fs ≥ 75th % and ≤ 25th %	54 (0.9%)	44 (3.5%)	7 (4.6%)	1 (0.9%)
Total	6336 (100%)	1240 (100%)[a]	153 (100%)[b]	107 (100%)

Note. Factor scores (fs) were calculated in 1991, 1993, and 1997. A subject was assigned to a group on the basis of his or her lowest or highest score on these three occasions. Subjects who scored above the 75th percentile on one occasion and below the 25th percentile on another were classified in a separate group.
[a]For 16 twins and siblings who participated in the CIDI, a factor score is missing; [b]For one subject who refused to participate, a factor score is missing.

pair. Twelve of them had not returned a questionnaire. Five participants had filled out a questionnaire, but missed items on the scales used to calculate the factor scores. Mean age of the participants at the time of the interview was 28.3 years.

Correlations within and between the personality and psychopathology dimensions were somewhat higher in the selected sample than in the total population. The highest correlations in the selected population were found between neuroticism and anxiety—namely, .80 in men and .84 in women. In the total population, these correlations were .69 and .75, respectively.

During the telephone interview, the following sections from the lifetime computerized version of the Composite International Diagnostic Interview (CIDI; World Health Organization, 1992) were administered to obtain lifetime DSM-IV diagnoses (American Psychiatric Association, 1994): Demographics (Sections A); Social Phobia, Agoraphobia, Panic Disorder, and Generalized Anxiety Disorder (D33 and further); Depression and Dysthymia (E); Mania Screen and Bipolar Affective Disorder (F); and Obsessive–Compulsive Disorder (K1–K22). The CIDI is a fully standardized diagnostic interview. No information on the reliability and validity of the Dutch version of the CIDI is available, but good reliability and validity have been reported for the American CIDI (Andrews & Peters, 1998). All interviewers were trained by the Dutch World Health Organization training center. The interviews were taped, and a trained clinician (C. M. M.) reviewed 126 interviews (10%) to check whether the interviewers had administered the CIDI appropriately. This appeared to be the case. However, it was apparent that questions regarding age of onset and age of recency were not reliably answered, because of comments made by the subjects such as "I have to guess" or "I do not know; I

suppose I was around __ years of age." This was also the case with respect to the number of episodes reported in major depression.

According to the diagnostic algorithm as obtained with the CIDI, subjects could be classified into one of three categories: "not affected," "affected," or "fulfilling the positive criteria, but not the exclusion criteria." The third category consisted of subjects with more than one anxiety disorder, subjects who exhibited symptoms of generalized anxiety disorder exclusively during a depressive episode, and subjects who fulfilled the criteria for an anxiety disorder but did not seek help for their symptoms. Subjects in this category were classified as "affected."

We analyzed data on major depression, dysthymia, generalized anxiety disorder, social phobia, panic disorder with or without agoraphobia, and agoraphobia without a history of panic disorder. Subjects with one of the latter three diagnoses were considered as one group, which is further referred to as "panic/agoraphobia." Subjects with bipolar disorder and/or obsessive–compulsive disorder without any other condition were excluded from the analyses (n = 8). Table 12.5 shows the number of subjects with no, one, two, three, four, or five diagnoses and the distribution of the disorders in these groups. Comorbidity was very common, especially in women or when an anxiety disorder was present.

MANOVAs were performed with the mean scores on the personality dimensions as dependent variables. In the first analysis, the diagnoses of major

TABLE 12.5. Frequency of the Number of Disorders in Men and in Women, with Specifications of Which Diagnoses Were Made

n disorders	Total (%)[a]	MDD (%)	Dys (%)	GAD (%)	Panic (%)	Social P (%)
Men						
0	454 (87.2)					
1	45 (8.6)	28 (5.4)	0	4 (0.8)	7 (1.3)	6 (1.1)
2	16 (3.1)	14 (2.7)	0	10 (1.9)	4 (0.8)	4 (0.8)
3	6 (1.1)	6 (1.1)	3 (0.6)	4 (0.8)	3 (0.6)	2 (0.4)
Total *n* men	521	48 (9.2)	3 (0.6)	18 (3.4)	14 (2.7)	12 (2.3)
Women						
0	532 (73.3)					
1	108 (14.8)	67 (9.2)	2 (0.3)	8 (1.1)	20 (2.7)	11 (1.5)
2	49 (6.7)	40 (5.5)	8 (1.1)	18 (2.5)	20 (2.7)	12 (1.6)
3	28 (3.8)	27 (3.7)	7 (1.0)	19 (2.6)	18 (2.5)	13 (1.8)
4	8 (1.1)	7 (1.0)	6 (0.8)	7 (1.0)	6 (0.8)	6 (0.8)
5	2 (0.3)	2 (0.3)	2 (0.3)	2 (0.3)	2 (0.3)	2 (0.3)
Total *n* women	727	143 (19.6)	25 (3.4)	54 (7.4)	66 (9.1)	44 (6.0)

Note. MDD, major depression; Dys, dysthymia; GAD, generalized anxiety disorder; Social P, social phobia.

[a]Percentages were always calculated from the total group of men (n = 521) or women (n = 727).

depression, dysthymia, social phobia, generalized anxiety disorder, or panic/agoraphobia constituted the independent variables. By including these variables in the model at the same time, we could control for comorbidity. The MANOVA showed that mean scores on the personality and psychopathology measures differed significantly between unaffected subjects and subjects with a diagnosis of major depression, social phobia, generalized anxiety disorder, or panic/agoraphobia ($p < .0005$) (Table 12.6). Only the scores of subjects diagnosed with dysthymia were not significantly different from those of the group without a disorder, although their scores were the same as or even higher than those of the other subjects with depression or an anxiety disorder. Interaction between variables was not included in the analysis, because power was too low to detect significant effects. Considering the results in more detail, the univariate tests demonstrated that subjects diagnosed with major depression, social phobia, generalized anxiety disorder, or panic/agoraphobia all differed significantly from the subjects without a disorder in their scores on neuroticism ($p \sim .005$). With regard to extraversion, only the subjects with social phobia or panic/agoraphobia showed decreased scores in comparison with the normal group ($p < .05$). On sensation seeking, subjects with diagnoses did not differ from normal controls.

TABLE 12.6. Mean Scores and Standard Deviations on Psychopathology and Personality Measures for Men and Women, with or without a DSM-IV Diagnosis of a Mood or Anxiety Disorder

	No diagnoses	MDD	Dys	GAD	Panic	Social P
Men						
BDI (*SD*)	–0.16 (0.72)	0.91 (0.97)	1.81 (0.91)	0.94 (0.96)	0.71 (0.78)	1.01 (1.28)
AD (*SD*)	–0.30 (0.88)	0.75 (0.91)	1.33 (0.07)	0.97 (0.57)	0.17 (1.33)	0.69 (0.80)
SoA (*SD*)	–0.26 (0.89)	0.58 (0.85)	0.89 (0.72)	0.81 (0.75)	0.35 (0.70)	0.82 (1.03)
Anx (*SD*)	–0.33 (1.00)	0.87 (1.09)	1.78 (0.23)	1.30 (0.61)	0.70 (0.87)	1.01 (1.36)
Neu (*SD*)	–0.40 (1.03)	0.75 (1.11)	1.50 (0.95)	1.06 (0.63)	0.35 (1.22)	1.16 (1.06)
Ext (*SD*)	0.14 (1.00)	–0.04 (1.26)	–0.95 (0.70)	0.03 (1.30)	–0.54 (0.88)	–0.48 (1.02)
SSS (*SD*)	0.26 (0.89)	0.32 (0.90)	0.42 (0.37)	0.53 (0.94)	–0.31 (0.78)	0.31 (0.89)
Women						
BDI (*SD*)	–0.01 (0.79)	0.92 (0.96)	1.63 (0.99)	1.29 (0.81)	0.76 (0.88)	1.00 (0.87)
AD (*SD*)	–0.06 (0.92)	0.96 (0.98)	1.43 (0.90)	1.28 (0.86)	0.99 (0.99)	1.38 (0.80)
SoA (*SD*)	–0.08 (0.93)	0.69 (1.05)	1.10 (1.06)	0.78 (1.04)	0.93 (0.92)	0.92 (0.95)
Anx (*SD*)	–0.17 (1.01)	0.92 (1.00)	1.68 (0.98)	1.39 (0.88)	0.91 (0.94)	1.20 (0.90)
Neu (*SD*)	–0.17 (1.03)	0.87 (0.97)	1.36 (0.99)	1.24 (0.91)	0.92 (0.88)	1.11 (0.86)
Ext (*SD*)	–0.03 (0.91)	–0.37 (0.90)	–0.82 (1.00)	–0.66 (0.88)	–0.44 (0.89)	–0.69 (0.74)
SSS (*SD*)	–0.41 (0.96)	–0.39 (0.97)	–0.55 (1.10)	–0.56 (0.96)	–0.32 (0.95)	–0.25 (0.90)

Note. Abbreviations as in Tables 12.2 and 12.5.

A second MANOVA, with the personality dimensions as independent variables and with the number of CIDI diagnoses as independent variable (zero, one, two, or three or more) did also reach significance ($p < .0001$) (Table 12.7). The univariate tests showed that neuroticism and extraversion, but not sensation seeking, were significantly different among the four groups of subjects. Figure 12.2 shows a positive relation between neuroticism and the number of disorders, and a negative relation between extraversion and the number of disorders.

DISCUSSION

We have presented results from two studies, which aimed to explore whether Eysenck's model or the tripartite model best describes the relation of neuroticism and extraversion to depressive and anxious psychopathology. Both models hypothesize that anxiety and depression are related to high neuroticism. Eysenck theorized that depression and anxiety are both also related to low extraversion. The tripartite model, on the other hand, hypothesizes that

TABLE 12.7. Mean Scores and Standard Deviations on Psychopathology and Personality Measures for Men and Women with Zero, One, Two, or Three or More Disorders

	Zero	One	Two	Three or more
Men				
BDI (*SD*)	–0.16 (0.72)	0.71 (0.91)	1.15 (1.00)	0.90 (0.90)
AD (*SD*)	–0.30 (0.88)	0.45 (1.01)	0.83 (0.92)	0.91 (0.66)
SoA (*SD*)	–0.26 (0.89)	0.39 (0.93)	0.83 (0.73)	0.75 (0.52)
Anx (*SD*)	–0.33 (1.00)	0.51 (1.14)	1.29 (0.81)	1.32 (0.47)
Neu (*SD*)	–0.40 (1.03)	0.43 (1.16)	1.24 (0.78)	1.03 (0.81)
Ext (*SD*)	0.14 (1.00)	–0.26 (1.31)	0.15 (1.19)	0.12 (1.12)
SSS (*SD*)	0.26 (0.89)	0.04 (0.85)	0.64 (1.10)	0.26 (0.46)
Women				
BDI (*SD*)	–0.01 (0.79)	0.66 (0.93)	0.93 (1.02)	1.33 (0.72)
AD (*SD*)	–0.06 (0.92)	0.74 (1.01)	1.14 (0.91)	1.38 (0.81)
SoA (*SD*)	–0.08 (0.93)	0.53 (0.98)	0.86 (1.01)	1.00 (0.99)
Anx (*SD*)	–0.17 (1.01)	0.65 (0.94)	0.93 (1.02)	1.47 (0.79)
Neu (*SD*)	–0.17 (1.03)	0.70 (0.98)	0.88 (0.91)	1.31 (0.81)
Ext (*SD*)	–0.03 (0.91)	–0.28 (0.94)	–0.40 (0.73)	–0.42 (0.92)
SSS (*SD*)	–0.41 (0.96)	–0.28 (0.93)	–0.75 (0.87)	–0.47 (1.02)

Note. Abbreviations as in Table 12.2.

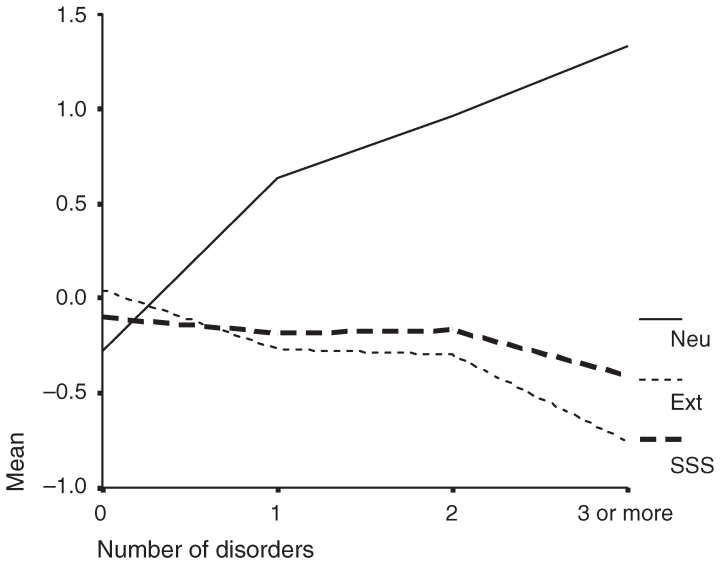

FIGURE 12.2. Relation between number of disorders and scores on neuroticism (Neu), extraversion (Ext), and sensation seeking (SSS).

depression, but not anxiety, is related to low positive affectivity, whereas anxiety is related to symptoms of autonomic hyperarousal. A second goal was to examine the relation of sensation seeking to anxious and depressive psychopathology. The analyses clearly showed that neuroticism is highly correlated with all measures of anxiety and depression. Low extraversion is also related to anxiety and depression, but to a lesser extent. Sensation seeking is not associated with anxiety and/or depression. In Study I, subjects with a score above the 95th percentile on anxious depression and anxiety had significantly higher sensation-seeking scores than normal controls ($p < .05$). This may simply reflect a consequence of multiple testing. The results support Eysenck's theory that depressive and/or anxious subjects score high on neuroticism and low on extraversion, as well as Zuckerman's hypothesis that sensation seeking, although weakly correlated with extraversion, is not related to anxiety and/or depression. These results thus suggest that the tripartite model can be rejected.

In all analyses, comorbidity between depression and anxiety was considered. In the first study, we used a cutoff score of the 95th percentile on the psychopathology questionnaires to divide subjects into groups consisting of normal controls, subjects with pure "disorders," and subjects with comorbid "disorders." Differences in personality measures with the normal controls were tested separately for all affected groups. In the second study, comorbidity was controlled for by including all disorders in the model, when personality

scores were compared between subjects with and without a disorder. Finally, the effect of comorbidity was directly investigated by analyzing the association between personality and the number of disorders. All analyses showed very similar results, although in the first study the division between the groups of affected and unaffected is based on self-report questionnaires and not on clinical criteria. The STAI, for example, has been shown not to assess anxiety only, but also depression and general negative affect (Bieling, Antony, & Swinson, 1998; Kennedy, Schwab, Morris, & Beldia, 2001). In our own sample, all four questionnaires (the BDI, the YASR, the STAI, and the ABV subscale for somatic anxiety) do not seem to distinguish between disorders (Table 12.6). Furthermore, the ABV subscale for somatic anxiety and the STAI—Trait version ask subjects to indicate how they generally feel, and the YASR asks about the last 6 months. Therefore, it is questionable whether state is measured with these questionnaires. However, the results are remarkably the same as the results of Study II. First, the relationship to the personality dimensions was the same for anxiety and depression measured either dimensionally or categorically. Second, neuroticism scores were higher and extraversion scores were lower when subjects suffered from more than one disorder.

Some results deserve further attention. In Study II, dysthymia was the only disorder that was not associated with neuroticism, although the neuroticism scores of subjects with dysthymia were comparable to those of the other groups diagnosed with a psychiatric disorder. This result might be a consequence of the low prevalence of dysthymia. Another explanation could be that the high neuroticism scores of subjects with dysthymia were due to comorbid disorders, since most of them also had another diagnosis—mainly major depression. This appears in accordance with Klein and Santiago's (2003) argument that the distinction between dysthymia and chronic depression is not meaningful. To our knowledge, there are no studies that have investigated the relation between neuroticism and dysthymia as a separate disorder while taking comorbidity into account.

Another interesting point is that in the first analysis of Study II, low extraversion only seemed related to social phobia and panic/agoraphobia and not to the other disorders, whereas this did not appear to be the case in Study I or in the second part of Study II. This might be due to a lack of power, since the trend was clearly the same for all disorders (Table 12.6). However, in other studies that took comorbidity into account, low extraversion did not appear to be associated with all disorders either. One of the studies found that low extraversion was related to social phobia and agoraphobia, but not to panic disorder and major depression (Bienvenu et al., 2001). Another study found that low extraversion was related to social phobia and major depression, but not to generalized anxiety disorder and panic disorder and/or agoraphobia (Brown et al., 1998). An explanation for these somewhat divergent findings could be that whereas neuroticism seems to be an independent risk factor, extraversion may interact with other risk factors—for example, life

events. In other words, subjects who score high on extraversion may be less sensitive to the effect of life events, or subjects with high extraversion may be less prone to adverse events that are associated with these disorders. For example, an extraverted, highly social individual may be at lower risk for a divorce. A recent study investigated the opposite of the latter hypothesis for sensation seeking, life events, and depression (Farmer et al., 2001). They hypothesized that subjects with high levels of sensation seeking might be more at risk for adverse events (which are related to major depression) because of their accident-prone behavior. This did not appear to be the case. However, this seems a promising direction of research. Interaction effects could lead to conflicting results, as in the case of the relation with low extraversion. When the group of affected subjects includes a relatively high number of patients who have experienced adverse effects and get a disorder because they are also low in extraversion, a relationship between extraversion and the disorder will be found. When, on the opposite, the group of affected subjects consists mainly of highly neurotic patients who already have a high risk of developing a psychiatric disorder, the relationship may be missed. This might explain why in our study low extraversion did not seem to be associated with all of the disorders we examined, while extraversion scores were found to decrease with the number of disorders. Subjects with comorbidity are probably more vulnerable to disorders (e.g., because of high neuroticism scores in combination with low extraversion scores) than subjects with a pure disorder.

The finding that sensation seeking is not related to anxiety and depression, but is weakly correlated to extraversion, is consistent with the view (which emerged after the development of the first version of the EPQ and the ABV) that impulsivity may reflect a third personality dimension independent of extraversion and neuroticism (Clark et al., 1994; Zuckerman, 1994).

Concerning the etiology of depression and anxiety, the linear relation between neuroticism and low extraversion on the one hand, and the number of disorders on the other, links nicely to the hypothesis that anxiety and depression are polygenic disorders with a partly shared common genetic background (Gray & McNaughton, 2000; Jardine, Martin, & Henderson, 1984; Kendler et al., 1995; Kendler, Neale, Kessler, Heath, & Eaves, 1993). The higher an individual's neuroticism score, and perhaps the lower the person's score on extraversion, the more genes the individual probably has that increase the vulnerability for depression and/or anxiety. This might also explain part of the comorbidity, as Bienvenu and colleagues (2001) have already suggested, because subjects scoring high on neuroticism and low on extraversion have an increased chance to have depression or an anxiety disorder—and, as a consequence, have a higher chance to have both disorders as well.

In addition, in both studies (although this was not formally tested), the relation between the personality dimensions and anxious or depressive psychopathology appeared to be the same for men and women. This signifies that

the higher prevalence rates for anxiety and depression in women are more likely to be explained by the higher neuroticism scores than by a different etiological background for anxiety and depression. This is confirmed by Goodwin and Gotlib (2004), who found that higher neuroticism scores in women might explain the gender difference in prevalence of major depression. The question of why women have higher neuroticism scores than men remains.

To conclude, high neuroticism and low extraversion are related to anxiety and depression, even when comorbidity between these disorders is taken into account. Sensation seeking seems an independent personality dimension, which is not associated with anxious and depressive psychopathology.

LOOKING FORWARD

The question of how to define psychiatric phenotypes has become more and more important during the last decades. This is partly induced by the realization that DSM categories cannot double as phenotypes when investigators are trying to discover robust genetic markers (Charney et al., 2002). The effect of a gene can, for instance, be missed when this gene leads to a pattern of symptoms that differs from a disorder as defined by the DSM-IV (for an illustration of this problem, see Hudziak, 2002). Considering the association of neuroticism and extraversion with anxious or depressive psychopathology, we would recommend that future gene-finding studies include these traits, in addition to specific disorders. The definitions of these traits are not fully etiologically based either, although neuroticism was originally hypothesized to be related to the visceral brain and extraversion to the ascending reticular arousal system (Eysenck, 1967). However, the Neuroticism and Extraversion scales consist of a broad spectrum of symptoms correlated with the more narrowly defined DSM-IV depression and anxiety disorders. A quantitative trait locus (QTL) responsible for a certain pattern of symptoms, which is not classified as a disorder according to the DSM-IV, might be detected when neuroticism and extraversion are investigated. Especially when these traits are analyzed simultaneously, an increase in statistical power for QTL detection might be realized (e.g., Boomsma & Dolan, 1998; Marlow et al., 2003). Furthermore, analyses of continuous traits such as neuroticism and extraversion have higher power to detect QTL effects than analyses of dichotomous traits such as depression. The demonstration of a relation between these personality traits and depression and anxiety forms a promising start for investigating whether genes that influence neuroticism and extraversion are also associated with anxious or depressive psychopathology. If candidate genes can be identified, it even becomes possible to examine what kinds of symptoms distinguish subjects with particular variants of those genes from other subjects. Ultimately, this strategy could lead to a more etiologically based classification system.

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